DECLARATION OF PAUL POLAKIS, Ph.D.

I, Paul Polakis, Ph.D., declare and say as follows:

1. I was awarded a Ph.D. by the Department of Biochemistry of the Michigan State University in 1984. My scientific Curriculum Vitae is attached to and forms part of this Declaration (Exhibit A).

2. I am currently employed by Genentech, Inc. where my job title is Staff Scientist. Since joining Genentech in 1999, one of my primary responsibilities has been leading Genentech's Tumor Antigen Project, which is a large research project with a primary focus on identifying tumor cell markers that find use as targets for both the diagnosis and treatment of cancer in humans.

3. I have read and understand the claims pending in the above-identified patent application, which are directed to a method of treating cancer in a mammal by administering to the mammal a therapeutically effective amount of an antibody that specifically binds to a polypeptide of SEQ ID NO: 2.

4. I have also read and understand the disclosure of WO 03/052119 A2, hereinafter referred to Baughn *et al.* Baughn *et al.* concerns polypeptides described as human transporters of ion channels and designated as "TRICH." One of the "TRICH" polypeptides, represented by SEQ ID NO:11, shows a 99.9% amino acid sequence identity to the polypeptide of SEQ ID NO:2 of the present application.

5. On page 59, line 9 – page 61, line 13, Baughn *et al.* states:

> "TRICH appears to play a role in transport, neurological, muscle, immunological and cell proliferative disorders. In the treatment of disorders associated with increased TRICH expression or activity, it is desirable to decrease the expression or activity of TRICH. In the treatment of disorders associated with decreased TRICH expression or activity, it is desirable to increase the expression or activity of TRICH.
>
> Therefore, in one embodiment, TRICH or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of TRICH. Examples of such disorders include, but are not limited to, a transport disorder such as akinesia, amyotrophic lateral sclerosis, ataxia telangiectasia, cystic fibrosis, Becker's muscular dystrophy, Bell's palsy, Charcot-Marie Tooth disease, diabetes mellitus, diabetes insipidus, diabetic neuropathy, Duchenne muscular dystrophy, hyperkalemic periodic paralysis, normokalemic periodic paralysis, Parkinson's disease, malignant hyperthermia, multidrug resistance, myasthenia gravis, myotonic dystrophy, catatonia, tardive dyskinesia, dystonias, peripheral neuropathy, cerebral neoplasms, prostate cancer, cardiac disorders associated with transport, e. g. , angina, bradyarrythmia, tachyarrythmia, hypertension, Long QT syndrome,

myocarditis, cardiomyopathy, nemaline myopathy, centronuclear myopathy, lipid myopathy, mitochondrial myopathy, thyrotoxic myopathy, ethanol myopathy, dermatomyositis, inclusion body myositis, infectious myositis, polymyositis, neurological disorders associated with transport, e. g. , Alzheimer's disease, amnesia, bipolar disorder, dementia, depression, epilepsy, Tourette's disorder, paranoid psychoses, and schizophrenia, and other disorders associated with transport, e. g. , neurofibromatosis, postherpetic neuralgia, trigeminal neuropathy, sarcoidosis, sickle cell anemia, Wilson's disease, cataracts, infertility, pulmonary artery stenosis, sensorineural autosomal deafness, hyperglycemia, hypoglycemia, Grave's disease, goiter, Cushing's disease, Addison's disease, glucose-galactose malabsorption syndrome, glycogen storage disease, hypercholesterolemia, adrenoleukodystrophy, Zellweger syndrome, Menkes disease, occipital horn syndrome, von Gierke disease, pseudohypoaldosteronism type1, Liddle's syndrome, cystinuria, iminoglycinuria, Hartup disease, Fanconi disease, and Bartter syndrome; a neurological disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis,cerebelloretinal hemangioblastomatosis,encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system including Down syndrome, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, seasonal affective disorder (SAD), akathesia, amnesia, catatonia, diabetic neuropathy, hemiplegic migraine, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, Tourette's disorder, progressive supranuclear palsy, corticobasal degeneration, and familial frontotemporal dementia; a muscle disorder such as cardiomyopathy, myocarditis, Duchenne's muscular dystrophy, Becker's muscular dystrophy, myotonic dystrophy, central core disease, nemaline myopathy, centronuclear myopathy, lipid myopathy, mitochondrial myopathy, infectious myositis, polymyositis, dermatomyositis, inclusion body myositis, thyrotoxic myopathy, ethanol myopathy, angina, anaphylactic shock,arrhythmias, asthma, cardiovascular shock, Cushing's syndrome, hypertension,

hypoglycemia, myocardial infarction, migraine, pheochromocytoma, and myopathies including encephalopathy, epilepsy,Kearns-Sayre syndrome, lactic acidosis, myoclonic disorder, ophthalmoplegia, acid maltase deficiency (AMD, also known as Pompe's disease), generalized myotonia, and myotonia congenita; an immunological disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodiclymphopenia withlymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves'disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma,Sjgren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic,protozoal, andhelminthic infections, and trauma; and a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnalhemoglobinuria, polycythemia vera, psoriasis, primarythrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, colon, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus."

(Emphasis added.)

6. On page 61, lines 24-29, Baughn *et al.* state:

"In a further embodiment, an antagonist of TRICH may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of TRICH. Examples of such disorders include, but are not limited to, those transport, neurological, muscle, immunological and cell proliferative disorders described above. In one aspect, an antibody which specifically binds TRICH may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissues which express TRICH."

(Emphasis added)

7. Thus , Baughn *et al.* suggest that TRICH polypeptides play a role in such diverse conditions as transport, neurological, muscle, immunological and cell proliferative disorders, including essentially any kind of cancer. They further suggest that such disorders can be prevented or treated either with TRICH polypeptides or with antagonists of TRICH polypeptides, such as antibodies which specifically bind TRICH. From other parts of the disclosure and the claims it appears that TRICH may be over- or under-expressed in such conditions, and in the case of under-expression, TRICH is used as a preventative or therapeutic agent, while in the case of over-expression, the treatment is performed with TRICH antagonists, such as antibodies which specifically bind TRICH. Baughn *et al.* have no data or other teaching indicating if the compound of SEQ ID NO: 11 is under- or over-expressed in any of these conditions.

8. Based on the disclosure discussed in paragraphs 5-7 above, in order to use antibodies that specifically bind the compound of SEQ ID NO: 11 for any therapeutic purpose, I would first need to determine if the polypeptide of SEQ ID NO: 11 is over-expressed or under-expressed in any transport, neurological, muscle, immunological or cell proliferative disorder. These broad classes of disorders include an extremely large number of diseases. Thus, for example, in addition to the cancer types (adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma) and cancers (cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, colon, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus) listed by Baughn *et al.*, cell proliferative disorders include a variety of other conditions, including actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnalhemoglobinuria, polycythemia vera, psoriasis, primarythrombocythemia, also listed by Baughn *et al.* Since Baughn *et al.* has no specific teaching about the involvement of the polypeptide of SEQ ID NO: 11 in any of such conditions, I would have no reason to prefer any type of disorders over other types, or any specific disease over any other.

9. Accordingly, in order to determine whether antibodies to the polypeptide of SEQ ID NO: 11 are useful in the treatment of any disease or disorder, I would need to investigate the involvement of the polypeptide of SEQ ID NO: 11 in a daunting number of transport, neurological, muscle, immunological and cell proliferative diseases until I find one where it seems to be involved, such as, under- or over-expressed. After finding a condition where the polypeptide of SEQ ID NO: 11 is over-expressed, I would need to examine whether the elevated expression levels of this polypeptide play a role in the pathology of the disease in question, and, if such role is confirmed, experimentally determine if antibodies specifically binding the polypeptide of SEQ ID NO: 11 are able to counteract such pathological role.

10. Anyone who has spent any time in a research laboratory, working on the identification of new drug targets and the development of drug candidates for the treatment of serious medical conditions would understand that the tasks outlined in paragraph 9 above would take more than a lifetime even for large groups of scientists. Accordingly, based on the disclosure of Baughn *et al.* I would not be able to use the

polypeptide of SEQ ID NO: 11 or an antibody specifically binding the polypeptide of SEQ ID NO: 11 for any therapeutic purpose, without a tremendous amount of experimentation, without any guarantee or even expectation that such experimentation would eventually yield a therapeutic use.

11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 2-21-2007

By: Paul Polakis

Paul Polakis, Ph.D.

SV 2245898 v1

EXHIBIT A

CURRICULUM VITAE

PAUL G. POLAKIS
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EDUCATION:

Ph.D., Biochemistry, Department of Biochemistry,
Michigan State University (1984)

B.S., Biology. College of Natural Science, Michigan State University (1977)

PROFESSIONAL EXPERIENCE:

2002-present	Staff Scientist, Genentech, Inc S. San Francisco, CA
1999- 2002	Senior Scientist, Genentech, Inc., S. San Francisco, CA
1997 -1999	Research Director Onyx Pharmaceuticals, Richmond, CA
1992- 1996	Senior Scientist, Project Leader, Onyx Pharmaceuticals, Richmond, CA
1991-1992	Senior Scientist, Chiron Corporation, Emeryville, CA.
1989-1991	Scientist, Cetus Corporation, Emeryville CA.
1987-1989	Postdoctoral Research Associate, Genentech, Inc., South SanFrancisco, CA.
1985-1987	Postdoctoral Research Associate, Department of Medicine, Duke University Medical Center, Durham, NC

1984-1985	Assistant Professor, Department of Chemistry, Oberlin College, Oberlin, Ohio
1980-1984	Graduate Research Assistant, Department of Biochemistry, Michigan State University East Lansing, Michigan

PUBLICATIONS:

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Responsive Gene Stra6 in Human Cancers and its Synergistic Induction by Wnt-1 and
Retinoic Acid. **Cancer Res** 61, 4197-4204.

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